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(54) Title: PREVENTION OF DEVELOPMENT OF DYSKINESIAS

(57) Abstract: The present invention relates to the prevention of the development of sensitization caused by chronic use of dopaminergic agents using an alfa2-adrenoceptor antagonist or a pharmaceutically acceptable ester or salt thereof.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/FI 01/00989

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/4174 A61K31/4164 A61K31/4178 A61P25/14 A61P25/00
 //C07D233/58,C07D233/00,C07D233/22,C07D319/20,C07D405/04,
 C07D307/85

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, BIOSIS, CHEM ABS Data, EMBASE, MEDLINE, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BRIAN HENRY PHD ET AL: "The alpha 2-adrenergic receptor antagonist idazoxan reduces dyskinesia and enhances anti-parkinsonian actions of L-Dopa in the MPTP-lesioned primate model of parkinson's disease" MOVEMENT DISORDERS, vol. 14, no. 5, 1999, pages 744-753, XP002902469 the whole document	1-6
X	GRONDIN R ET AL : "Noradrenoceptor antagonism with idazoxan improves L-dopa-induced dyskinesias in MPTP monkeys." NAUNYN-SCHMIEDEBERG'S ARCH PHARMACOL, vol. 361, 2000, pages 181-186, XP002902470 the whole document	1-6
	-/-	

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

*** Special categories of cited documents :**

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

8 May 2002

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13. 06. 2002

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/FI 01/00989

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Section Ch, Week 199838 Derwent Publications Ltd., London, GB; Class B02, AN 1998-439852 XP002902471 abstract & FR 2 759 291 A (FABRE MEDICAMENT SA) 14 August 1998 (1998-08-14)</p> <p>---</p>	1-6
P,X	<p>DATABASE STN INTERNATIONAL [Online] file medline; RASCOL O ET AL : "Idazoxan, an alpha 2-antagonist and L-dopa-induced dyskinesias in patients with parkinson's disease." retrieved from MEDLINE, accession no. 2001433881 Database accession no. 21374324</p> <p>XP002902472 abstract & MOVEMENT DISORDERS , vol. 16, no. 4, July 2001 (2001-07), pages 708-713,</p> <p>---</p>	1-6
P,X	<p>DATABASE STN INTERNATIONAL [Online] file medline; FOX S H ET AL: "Neutral mechanisms underlying peak-dose dyskinesia induced by levodopa and apomorphine are distinct: Evidence from the effects of the alpha 2-adrenoceptor antagonist idazoxan." retrieved from MEDLINE, accession no. 2001433872 Database accession no. 21374315 XP002902473 abstract & MOVEMENT DISORDERS, vol. 16, no. 4, July 2001 (2001-07), pages 642-650,</p> <p>---</p> <p style="text-align: center;">-/--</p>	1-6

INTERNATIONAL SEARCH REPORT

International Application No

PCT/FI 01/00989

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 2001 SAVOLA J M ET AL: "JP-1730, a novel alpha2-adrenergic antagonist, reduces L-DOPA-induced dyskinesia in animal models of Parkinson's disease." Database accession no. PREV200100499788 XP002902474 abstract & SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 27, no. 1, 2001, page 531 31st Annual Meeting of the Society for Neuroscience; San Diego, California, USA; November 10-15, 2001 ISSN: 0190-5295 -----</p>	1-6

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-6
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 1-6

Present claims 1-2 relate to a method defined by reference to a desirable property of the compounds to be used in the method, namely antagonism of the alpha 2-adrenoreceptor. The claims 1-2 cover the use of all compounds having this property, whereas the application provides support within the meaning of Art. 6 PCT and disclosure within the meaning of Art. 5 PCT for only a very limited number of such compounds.

Independent of the above reasoning, the claims 1-2 also lack clarity (Art. 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. This lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Specifically, the term "alpha 2-adrenoreceptor antagonist" apparently relates to a very large amount of different compounds, which do not necessarily have to be defined as alpha 2-adrenoreceptor antagonists, thus rendering it impossible to perform a complete search.

Furthermore, the claims 1-6 are not clear and concise according to Article 6 PCT with respect to the phrase "sensitization caused by chronic use of dopaminergic agents." While this expression is unambiguous in itself, it makes it impossible to perform a complete search since it relates to sensitization caused by chronic use of all agents that are dopaminergic, including ones that do not necessarily have to be referred to as dopaminergic agents.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to use of the compounds mentioned in claims 3-6 for prevention of development of sensitizational conditions caused by chronic use of the specific dopaminergic agents mentioned in the description, i.e. L-dopa, amphetamine, cocaine and apomorphine.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.